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OVERVIEW OF INFORMATION NECESSARY FOR PREMARKET NOTIFICATION SUBMISSIONS FOR ENDOSSEOUS IMPLANTS

I. General requirements for a Premarket Notification Submission for Endosseous Implants

A. Intended Use of the Device

1. For implantation into the fully edentulous ridge for the support of a dental prosthesis

2. For implantation into the partially edentulous ridge for the support of a dental prosthesis

3. For single tooth use

B. Device Description

1. Design characteristics

   a. Screw, cylindrical or blade type implants

   b. Hexed top or other anti-rotational feature

   c. Size: diameter, length, other dimensions particularly in regions that interface with other components

2. Accessory components and instruments

   a. Abutments
   b. Laboratory components
   c. Drills, burs, screwdrivers

3. Material composition of all components

   a. Complete chemical composition

   b. Reference to any voluntary standards to which the finished device material specifications conform (e.g. ASTM F136 or titanium alloy)

   c. Mechanical properties of the material if it does not conform to a specific standard

4. Engineering diagrams of all components; these diagrams should include tolerances

C. Sterilization information

1. If the device will be provided sterile, information is requested based on the ODE Bluebook policy regarding sterilization; the basic information requested is listed below

a. Sterilization methods and procedures

b. Method employed to validate sterility

c. Sterility assurance level (SAL) for the device; an SAL of 10^{-6} or better is deemed acceptable

d. Packaging used to maintain the device's sterility

e. Description of the method used to determine whether or not the device is pyrogen free if it is intended to be pyrogen free

f. Radiation dose if radiation sterilization is used

g. Ethylene oxide residue level remaining on the device if this sterilization method is used

2. If the device is not intended to be provided sterile, the instructions for use should include the proper sterilization parameters that should be used.

D. Labeling, instructions for use and promotional materials

II. Additional information requested when needed

A. Mechanical testing of device

1. Mechanical testing is requested for the following:

a. Angled abutments
b. Implant or abutment designs that are significantly different from those of predicate devices
c. New design feature or technological characteristic

2. Testing should be performed on the finished device (i.e., components that have undergone the same manufacturing process as the finished device that is to be marketed)

3. Test results are compared to those of other predicate devices and to conditions that would be expected during the function of the device *in vivo*

4. Static compressive and shear testing:

   a. Testing should be performed on assembled device (i.e., with the abutment attached to the implant)

   b. Test should be set-up such that the implant/abutment system experiences both compressive and shear (lateral) forces; test conditions should mimic actual use as much as possible

   c. Testing should be performed in a simulated physiological solution at 37°C

   d. Five to ten samples should be tested

   e. Test results are compared to the maximum static compressive/shear force tolerated by other similar predicate devices, and to loads that would be exerted on the implant when in function

5. Fatigue testing in compression and shear:

   a. The criteria listed above for the static testing should also be used for the fatigue testing

   b. The test must be performed out to 5×10^6 cycles, demonstrating an expected lifetime (without failure) of 5 years.

   c. Preferably, an S-N curve should be generated. However, in the past, we have sometimes allowed applicants to identify the maximum load at which the implant-abutment system can withstand 5 million cycles. At least 5 samples should be tested to verify that the system can survive 5 million cycles at this load. The loads exerted on the abutment-implant system should be above reasonable loads that would be encountered *in situ*.

d. Particularly for angled abutments, the testing should be performed at the greatest angulation intended (i.e., the worst case scenario). The maximum acceptable angulation without requiring clinical studies is 30 degrees.

e. Testing should be performed in a simulated physiological solution at 37°C

f. The critical failure point and the location of failure initiation should be identified. Failure is defined as material yielding, deformation or fracture.

g. Test results are compared to the fatigue strength of other similar predicate devices, and to loads that would be exerted on the implant when in function

B. Corrosion testing

1. Corrosion testing is requested when the implant system includes components fabricated from dissimilar metals.

2. A guidance document was developed on the type of information needed for galvanic corrosion testing and the test conditions that should be used. The information requested includes the following:

a. Corrosion potential of each metal or alloy

b. Couple potential for the assembled dissimilar metal implant system

c. Corrosion rate for the assembled dissimilar metal implant system

d. Tests should be performed in a simulated physiological solution at 37°C

e. Passivated (i.e., finished device condition) and nonpassivated metal surfaces should be evaluated

C. Biocompatibility testing (toxicological tests)

1. Requested when a new material or material component is used that has not been identified in a predicate device or in another medical device

2. Request that biocompatibility testing for the new material and/or the finished device be performed according to the *Tripartite Biocompatibility Guidance.* The following tests should be performed:

   a. Irritation
   b. Sensitization assay
   c. Cytotoxicity
   d. Acute systemic toxicity
   e. Hemocompatibility
   f. Pyrogenicity
   g. Implantation test
   h. Mutagenicity test
   i. Subchronic toxicity
   j. Carcinogenesis bioassay

D. Characterization of any coatings used

1. *The Calcium Phosphate Coating Draft Guidance for Preparation of FDA Submissions for Orthopedic and Dental Endosseous Implants* was developed jointly by the Orthopedic Devices Branch and the Dental Devices Branch.

2. The document outlines the type of information that should be submitted to adequately characterize calcium phosphate coatings. The following information is requested:

   (All requested data and testing should be performed on the finished device or on a specimen that has undergone the same manufacturing process intended for the marketed device, including the sterilization process)

   a. The type of deposition process used and the post-deposition heat treatment (if any)

   b. An elemental analysis for the powder and coating, noting any impurities such as heavy metals (i.e., As, Cd, Hg, and Pb)

   c. The calcium/phosphorous ratio (Ca/P) in atomic percent for the powder and coating forms. The Ca/P ratio should be within 1.66 to 1.67 and 1.67 to 1.76 for the powder and coating forms, respectively.

d. The x-ray diffraction spectra of the powder and coating in terms of relative intensity versus diffraction angle. For hydroxylapatite (HA) coatings, the hydroxylapatite and tricalcium phosphate JCPDS (Joint Committee on Powder Diffraction Standards) standards must be individually superimposed on the spectra for the powder and coating.

e. The percent (weight percent) of each component and the percent crystallinity of the powder and coating after it has undergone the full manufacturing process

For hydroxylapatite (HA) coatings:

(1) The minimum crystallinity of the HA component of the coating that has been identified in predicate devices is 70%. The minimum crystallinity of the total coating that has been identified in predicate devices is 62%. If the crystallinity of the HA portion of the coating is less than 70% or if the total crystallinity of the coating is less than 62%, additional information may be requested.

(2) If the purity of the powder is less than 95% or if the coating contains less than 90% of the labeled compound (e.g., hydroxylapatite), the labeling for the implant should identify all major compounds present in the coating.

f. The infrared spectra of the powder and the coating in terms of percent transmittance versus wavenumber. The characteristic absorption bands and radical groups for the Ca-P compound should be identified.

g. The solubility products of the powder and coating, in simulated physiological solution at 37°C

h. The dissolution rate of the powder and coating, in a simulated physiological buffered solution at 37°C and a pH of 7.3

i. The coating thickness and the portion of the device that is to be coated.

j. Photomicrographs of the coating and coating substrate interface at 100X magnification

(2) Methods, materials, raw data, a photograph or drawing of the set-up, a failure report, and magnified photographs of the failure regions should be included

(3) Because this testing cannot be performed on the actual device, we request that testing be performed on a sample that has undergone the same manufacturing process as the finished device

g. The abrasion characteristics of the coated device. A method for abrasion testing is given in the *Guidance Document for Testing Orthopedic Implants with Modified Metallic Surfaces Apposing Bone or Bone Cement.* The testing should be performed according to the recommended procedures. If another method is used, adequate justification for its use should be provided.

E. Test reports should include a standard deviation analysis. The report should include the detailed test protocol, methods for sample preparation, raw data, a photograph or drawing of the test set-up, a failure report and magnified photographs of the failure regions.

F. Animal and clinical studies

1. Animal and/or clinical studies are requested if the diameter of an implant is less than 3.25 mm, if the length is less than 7 mm and if the angulation of the abutment is greater than 30°. These particular numbers were derived based on predicate devices.

2. Animal and/or clinical studies may also be requested if the design of the device is significantly different from those of other predicate devices.